

Toby Port

Access DB#

72797

RECEIVED
SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Rubina (STIC) Examiner #: 69826 Date: 8/17/02
Art Unit: 1614 Phone Number 30 84724 Serial Number: 101091591
Mail Box and Bldg/Room Location: 2D01 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search attached compound
of formula I.

Thanks
Rubina

Point of Contact:
Toby Port
Technical Info. Specialist
CM1 6A04
703-308-3534

STAFF USE ONLY

	Type of Search	Vendors and cost where applicable
Searcher: _____	NA Sequence (#) _____	STN <u>391</u>
Searcher Phone #: _____	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) <u>1</u>	Questel/Orbit _____
Date Searcher Picked Up: <u>8/13</u>	Bibliographic _____	Dr.Link _____
Date Completed: <u>8/15</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: <u>20</u>	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: <u>90</u>	Other _____	Other (specify) _____

=> file reg; d stat que l16

FILE 'REGISTRY' ENTERED AT 16:00:24 ON 15 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0
DICTIONARY FILE UPDATES: 14 AUG 2002 HIGHEST RN 443957-06-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

L7 SCR 1007
L8 SCR 1236
L12 STR

N—G2—NH—Cb—NH—G2—N
1 2 3 4 5 6 7

REP G2=(3-6) CH2

NODE ATTRIBUTES:

NSPEC IS RC AT 1
NSPEC IS RC AT 7
DEFAULT MLEVEL IS ATOM
GGCAT IS SAT AT 4
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M3-X10 C AT 4

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 7

STEREO ATTRIBUTES: NONE

L14 SCR 1839

~~L16~~ ~~L19~~ SEA FILE=REGISTRY SSS FUL L12 AND L7 AND L8 NOT L14

=> file caplus; d que nos l19

FILE 'CAPLUS' ENTERED AT 16:21:02 ON 15 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN. Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is

strictly prohibited.

FILE COVERS 1907 - 15 Aug 2002 VOL 137 ISS 7
FILE LAST UPDATED: 14 Aug 2002 (20020814/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

```
L7          SCR 1007
L8          SCR 1236
L12         STR
L14         SCR 1839
L16         19 SEA FILE=REGISTRY SSS FUL L12 AND L7 AND L8 NOT L14
L19         18 SEA FILE=CAPLUS ABB=ON PLU=ON L16
```

=> file uspatfull; d que nos l22

FILE 'USPATFULL' ENTERED AT 16:02:13 ON 15 AUG 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 15 Aug 2002 (20020815/PD)
FILE LAST UPDATED: 15 Aug 2002 (20020815/ED)
HIGHEST GRANTED PATENT NUMBER: US6434748
HIGHEST APPLICATION PUBLICATION NUMBER: US2002112271
CA INDEXING IS CURRENT THROUGH 15 Aug 2002 (20020815/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 15 Aug 2002 (20020815/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2002
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2002

```
>>> USPAT2 is now available.  USPATFULL contains full text of the  <<<
>>> original, i.e., the earliest published granted patents or  <<<
>>> applications.  USPAT2 contains full text of the latest US  <<<
>>> publications, starting in 2001, for the inventions covered in  <<<
>>> USPATFULL.  A USPATFULL record contains not only the original  <<<
>>> published document but also a list of any subsequent  <<<
>>> publications.  The publication number, patent kind code, and  <<<
>>> publication date for all the US publications for an invention  <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL  <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc.  <<<
```

```
>>> USPATFULL and USPAT2 can be accessed and searched together  <<<
>>> through the new cluster USPATALL.  Type FILE USPATALL to  <<<
>>> enter this cluster.  <<<
>>>  <<<
>>> Use USPATALL when searching terms such as patent assignees,  <<<
>>> classifications, or claims, that may potentially change from  <<<
>>> the earliest to the latest publication.  <<<
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L7          SCR 1007
L8          SCR 1236
L12         STR
```

L14 SCR 1839
 L16 19 SEA FILE=REGISTRY SSS FUL L12 AND L7 AND L8 NOT L14
 L22 8 SEA FILE=USPATFULL ABB=ON PLU=ON L16

=> dup rem 119 122
 FILE 'CAPLUS' ENTERED AT 16:02:49 ON 15 AUG 2002
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATFULL' ENTERED AT 16:02:49 ON 15 AUG 2002
 CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
 PROCESSING COMPLETED FOR L19
 PROCESSING COMPLETED FOR L22

L23 19 DUP REM L19 L22 (7 DUPLICATES REMOVED)
 ANSWERS '1-18' FROM FILE CAPLUS
 ANSWER '19' FROM FILE USPATFULL

=> a ibib abs hitstr 123 1-19

L23 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
 ACCESSION NUMBER: 2002:425423 CAPLUS
 DOCUMENT NUMBER: 136:395970
 TITLE: Method and composition for the treatment of diarrhea
 and gastrointestinal spasms
 INVENTOR(S): Bergeron, Raymond J.
 PATENT ASSIGNEE(S): University of Florida, USA
 SOURCE: U.S., 8 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6399662	B1	20020604	US 2000-734660	20001213

OTHER SOURCE(S): MARPAT 136:395970

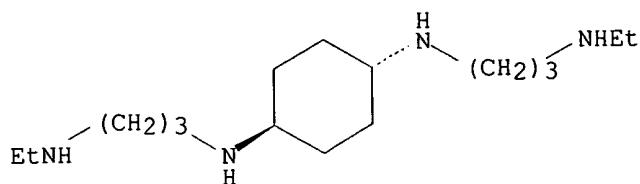
AB Anti-diarrheal and/or gastrointestinal anti-spasmodic pharmaceutical compns. contg. a polyamine of the formula: R1-N1(R2)-(CH2)x-N2H-Q-N3H-(CH2)y-N4(R3)-R4(I) wherein: R1, R2, R3 and R4 may be the same or different and are H, alkyl, cycloalkyl or aralkyl having from 1 to 12 carbon atoms, or a heterocyclic group having from 3 to 10 atoms wherein the hetero atom is said N1 or N4; Q is a cycloalkyl group having from 3 to 10 carbon atoms; x is an integer from 3 to 6, inclusive; and y is an integer from 3 to 6, inclusive; or, a salt thereof with a pharmaceutically acceptable acid; and a pharmaceutically acceptable carrier therefor as well as methods of treatment utilizing the polyamines are disclosed. N,N'-bis[3-(ethylamino)propyl]-trans-1,4-cyclohexanediamine, prepd. from trans-1,4-diaminocyclohexane, is shown to be effective in the castor oil-induced diarrhea model in rats and also in controlling irritable bowel syndrome in rats.

IT 177798-16-2P 323582-94-1P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (bis[ethylamino)propyl]cyclohexanediamine for treatment of diarrhea and gastrointestinal spasms)

RN 177798-16-2 CAPLUS
 CN 1,4-Cyclohexanediamine, N,N'-bis[3-(ethylamino)propyl]-, trans- (9CI) (CA

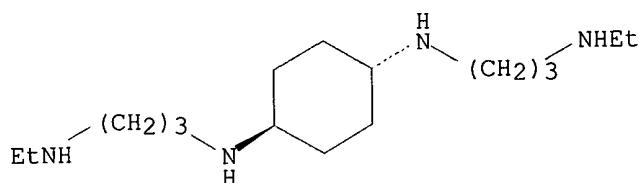
INDEX NAME)

Relative stereochemistry.



RN 323582-94-1 CAPLUS
 CN 1,4-Cyclohexanediamine, N,N'-bis[3-(ethylamino)propyl]-,
 tetrahydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● 4 HCl

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
 ACCESSION NUMBER: 2001:91511 CAPLUS
 DOCUMENT NUMBER: 134:147439
 TITLE: Preparation of analogs of biologically active,
 naturally occurring polyamines, their pharmaceutical
 compositions and methods of treatment
 INVENTOR(S): Bergeron, Raymond J., Jr.
 PATENT ASSIGNEE(S): University of Florida, USA
 SOURCE: U.S., 18 pp., Cont.-in-part of U.S. 5,342,945.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 6
 PATENT INFORMATION:

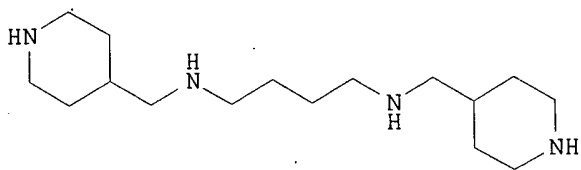
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6184232	B1	20010206	US 1993-80642	19930622
US 5091576	A	19920225	US 1988-210520	19880623
US 5342945	A	19940830	US 1992-834345	19920212
US 6147262	A	20001114	US 1992-986576	19921207
US 5455277	A	19951003	US 1993-162776	19931208
US 5866613	A	19990202	US 1995-478041	19950607
US 5866613	B1	20000314		
US 5679682	A	19971021	US 1996-714284	19960918
US 5681837	A	19971028	US 1996-714287	19960918

US 5827894	A	19981027	US 1996-714296	19960918
US 6034139	A	20000307	US 1996-714294	19960918
JP 10168067	A2	19980623	JP 1997-329524	19971113
JP 2945360	B2	19990906		
US 6362232	B1	20020326	US 2000-645510	20000825
US 6342534	B1	20020129	US 2000-688386	20001017
US 2002094990	A1	20020718	US 2001-985804	20011106

PRIORITY APPLN. INFO.:

US 1986-936835	B2	19861202
US 1987-66227	B2	19870625
US 1988-210520	A3	19880623
US 1992-834345	A2	19920212
JP 1994-240744	A3	19890623
US 1992-986576	A1	19921207
US 1993-80642	A1	19930622
US 1993-162776	A3	19931208
US 1995-474911	B1	19950607
US 1995-478040	B1	19950607
US 1995-481860	B1	19950607
US 1995-481864	B1	19950607
US 2000-645510	A1	20000825

OTHER SOURCE(S): MARPAT 134:147439
GI



I

AB Polyamines, R1R2N1A(N2R3B)a(N3R4C)bN4R5R6 [R1 - R6 = H, alkyl, aryl, arylalkyl, cycloalkyl, optionally having an alkyl chain interrupted by at least one etheric oxygen atom, wherein at least one of R1 and R2 and at least one of R5 and R6 .noteq. H; N1, N2, N3 and N4 are nitrogen atoms capable of protonation at physiol. pH's; a, b = from 1 - 4; A, B, C = bridging groups which effectively maintain the distance between the nitrogen atoms], or a salt thereof with a pharmaceutically acceptable acid such that the polyamines: (i) are capable of uptake by a target cell upon administration thereof to a human or non-human animal; and (ii) upon uptake by the target cell, competitively bind via an electrostatic interaction between the pos. charged nitrogen atoms to substantially the same biol. counter-anions as the intracellular natural polyamines in the target cell; the polyamines, upon binding to the biol. counter-anion in the cell, function in a manner biol. different than the intracellular polyamines, the polyamines not occurring in nature; as well as pharmaceutical compns. embodying the polyamines and methods of treating patients requiring anti-neoplastic therapy. Thus, polyamine I was prepd. from 4-(aminomethyl)piperidine via protection with mesitylenesulfonyl chloride in CH2Cl2 contg. NaOH, N-alkylation with 1,4-dibromobutane, in DMF contg. NaH and NaI, and deprotection with HBr in HOAc/PhOH/CH2Cl2. I showed antineoplastic activity (IC50 = 2 .mu.M at 48 h and 0.2 .mu.M at 96 h) against L1210 cells.

IT 221636-83-5P, trans-N,N'-Bis[4-(N-ethylamino)butyl]-1,4-cyclohexanediamine tetrahydrochloride 323582-89-4P, cis-N,N'-Bis[4-(N-ethylamino)butyl]-1,4-cyclohexanediamine tetrahydrochloride 323582-94-1P, trans-N,N'-Bis[4-(N-

ethylamino)propyl]-1,4-cyclohexanediamine tetrahydrochloride

323582-99-6P, cis-N,N'-Bis[4-(N-ethylamino)propyl]-1,4-cyclohexanediamine tetrahydrochloride 323583-02-4P

323583-05-7P, trans-N,N'-Bis[4-(N-ethylamino)propyl]-1,3-cyclohexanediamine tetrahydrochloride

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

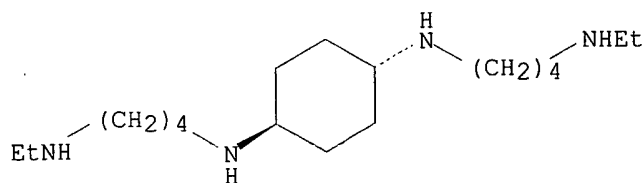
BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and antineoplastic activity of analogs of biol. active, naturally occurring polyamines)

RN 221636-83-5 CAPLUS

CN 1,4-Cyclohexanediamine, N,N'-bis[4-(ethylamino)butyl]-, tetrahydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

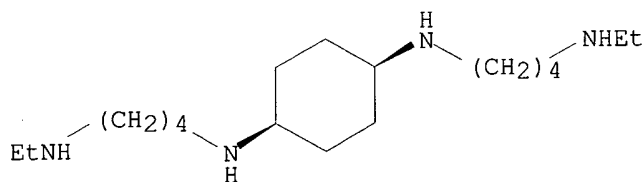


● 4 HCl

RN 323582-89-4 CAPLUS

CN 1,4-Cyclohexanediamine, N,N'-bis[4-(ethylamino)butyl]-, tetrahydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

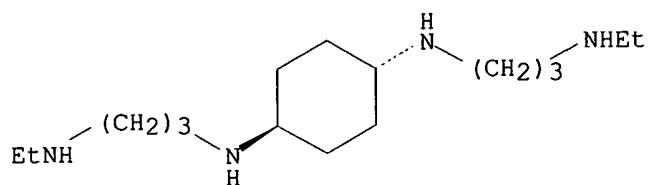


● 4 HCl

RN 323582-94-1 CAPLUS

CN 1,4-Cyclohexanediamine, N,N'-bis[3-(ethylamino)propyl]-, tetrahydrochloride, trans- (9CI) (CA INDEX NAME)

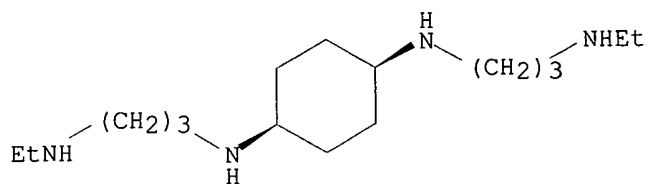
Relative stereochemistry.



●4 HCl

RN 323582-99-6 CAPLUS
 CN 1,4-Cyclohexanediamine, N,N'-bis[3-(ethylamino)propyl]-,
 tetrahydrochloride, cis- (9CI) (CA INDEX NAME)

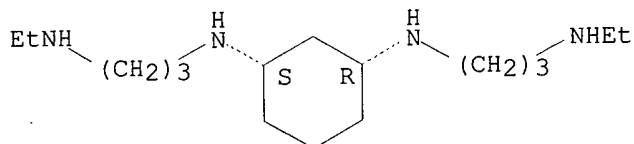
Relative stereochemistry.



●4 HCl

RN 323583-02-4 CAPLUS
 CN 1,3-Cyclohexanediamine, N,N'-bis[3-(ethylamino)propyl]-,
 tetrahydrochloride, (1R,3S)-rel- (9CI) (CA INDEX NAME)

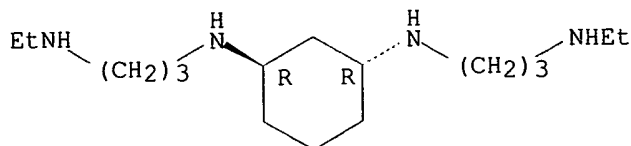
Relative stereochemistry.



●4 HCl

RN 323583-05-7 CAPLUS
 CN 1,3-Cyclohexanediamine, N,N'-bis[3-(ethylamino)propyl]-,
 tetrahydrochloride, (1R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● 4 HCl

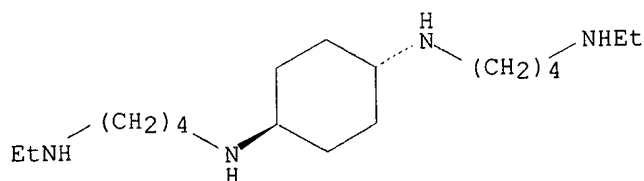
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
 ACCESSION NUMBER: 1999:635474 CAPLUS
 DOCUMENT NUMBER: 131:252594
 TITLE: Hydroxy polyamines and therapeutic uses thereof
 INVENTOR(S): Bergeron, Raymond J. , Jr.
 PATENT ASSIGNEE(S): University of Florida Research Foundation, Inc., USA
 SOURCE: U.S., 21 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5962533	A	19991005	US 1996-595877	19960206

OTHER SOURCE(S): MARPAT 131:252594
 AB Polyamines HN1(R1)ALK1N2(R2)ALK2N3(R3)ALK3N4(R4)H [R1, R4 = alkyl, aryl, aralkyl, cycloalkyl, with optional .gtoreq.1 etheric O in alkyl chain; R2, R3 = H, R1, R4; N1-N4 = (un)protonated N; ALK1-ALK3 = C1-4 (un)branched alkylene], and salts and stereoisomers thereof, are disclosed.
 Pharmaceutical compns. and therapeutic methods of treatment of cancer and diarrhea using the compds. are also disclosed.
 IT 177798-15-1 177798-16-2
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (hydroxypolyamines and therapeutic uses thereof)
 RN 177798-15-1 CAPLUS
 CN 1,4-Cyclohexanediamine, N,N'-bis[4-(ethylamino)butyl]-, trans- (9CI) (CA INDEX NAME)

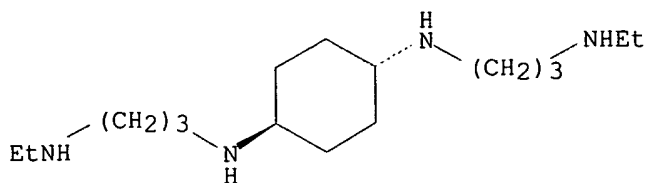
Relative stereochemistry.



RN 177798-16-2 CAPLUS
 CN 1,4-Cyclohexanediamine, N,N'-bis[3-(ethylamino)propyl]-, trans- (9CI) (CA INDEX NAME)

INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
 ACCESSION NUMBER: 1999:212803 CAPLUS
 DOCUMENT NUMBER: 130:252086
 TITLE: Preparation of conformationally restricted spermine analogs as antineoplastic agents
 INVENTOR(S): Frydman, Benjamin J.; Marton, Laurence J.; Reddy, Vendohar K.; Valasinas, Aldonia L.; Witiak, Donald T.
 PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
 SOURCE: U.S., 41 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5889061	A	19990330	US 1997-951015	19971015
US 6392098	B1	20020521	US 1999-280278	19990329

PRIORITY APPLN. INFO.: US 1997-951015 A1 19971015

OTHER SOURCE(S): MARPAT 130:252086

AB Z(NHZ1NHR)2 [I; R = H or alk(en)yl; Z = BAB; A, Z1 = (cyclo)alk(en)ylene, arylene; B = bond or alk(en)ylene] were prepd. Thus, N,N'-bis(mesitylsulfonyl)-cis-1,2-cyclobutanediamine (prepn. given) was N-alkylated by Br(CH2)3NEtSO2C6H2Me3-2,4,6 to give, after deprotection, Z[NH(CH2)3NHET]2 (Z = cis-1,2-cyclobutylene). Data for biol. activity of I were given in graphic form.

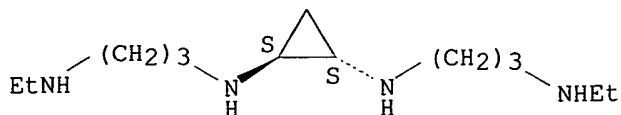
IT 206991-29-9P 206991-30-2P 206991-50-6P
 206991-51-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of conformationally restricted spermine analogs as antineoplastic agents)

RN 206991-29-9 CAPLUS

CN 1,2-Cyclopropanediamine, N,N'-bis[3-(ethylamino)propyl]-, tetrahydrochloride, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

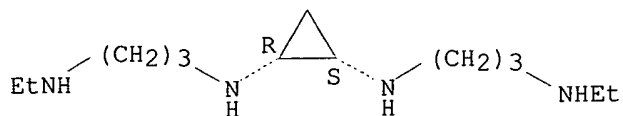


●4 HCl

RN 206991-30-2 CAPLUS

CN 1,2-Cyclopropanediamine, N,N'-bis[3-(ethylamino)propyl]-, tetrahydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

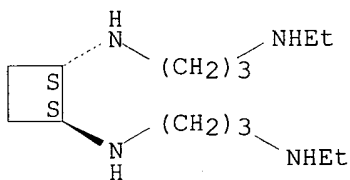


●4 HCl

RN 206991-50-6 CAPLUS

CN 1,2-Cyclobutanediamine, N,N'-bis[3-(ethylamino)propyl]-, tetrahydrochloride, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

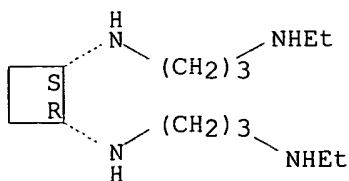


●4 HCl

RN 206991-51-7 CAPLUS

CN 1,2-Cyclobutanediamine, N,N'-bis[3-(ethylamino)propyl]-, tetrahydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● 4 HCl

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
 ACCESSION NUMBER: 1999:205324 CAPLUS
 DOCUMENT NUMBER: 130:252249
 TITLE: Methods and compositions for the treatment of neurodegeneration
 INVENTOR(S): Bergeron, Raymond J., Jr.; Borg, Stefan
 PATENT ASSIGNEE(S): University of Florida Research Foundation, Inc., USA; Sunpharm Corporation
 SOURCE: U.S., 21 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5886051	A	19990323	US 1995-554370	19951108

OTHER SOURCE(S): MARPAT 130:252249

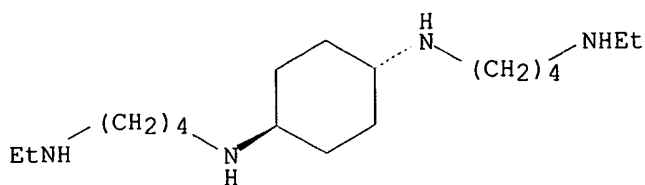
AB Methods and pharmaceutical compns. in unit dosage form for treating neurodegeneration in a human or nonhuman animal afflicted therewith wherein the active agent is a therapeutically effective amt. of a polyamine or a salt thereof with a pharmaceutically acceptable acid. E.g., N,N'-1,4-bis(2,4,6-trimethylbenzenesulfonyl)butanediylbis[4-(2,4,6-trimethylbenzenesulfonyl)piperidineethanamine], prepd. in 85% yield from N,N'-1,4-bis(2,4,6-trimethylbenzenesulfonyl)butanediamine and N,O-bis(2,4,6-trimethylbenzenesulfonyl)piperidineethanol, was hydrolyzed to give 68% N,N'-1,4-butanediylbis[4-piperidineethanamine]. Also prepd. were trans-1,4-cyclohexanediamines. Extensive data were given for the effectiveness of polyamines in treating cognitive disorders including expts. with human adults in the early stages of Alzheimer's disease.

IT **221636-83-5P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and cognition enhancing activity of polyamines)

RN 221636-83-5 CAPLUS

CN 1,4-Cyclohexanediamine, N,N'-bis[4-(ethylamino)butyl]-, tetrahydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● 4 HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
 ACCESSION NUMBER: 1982:407391 CAPLUS
 DOCUMENT NUMBER: 97:7391
 TITLE: Polyamine substituted cycloaliphatic compounds
 INVENTOR(S): Kluger, Edward W.; Su, Tien Kuei; Thompson, Teresa J.
 PATENT ASSIGNEE(S): Milliken Research Corp., USA
 SOURCE: U.S., 6 pp. Cont. of U.S. Ser. No. 925,009, abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4321354	A	19820323	US 1980-183405	19800902
PRIORITY APPLN. INFO.:			US 1977-850460	19771110
			US 1978-925009	19780717

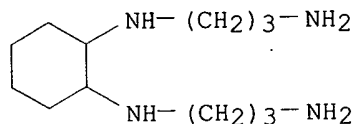
AB Cycloaliph. triamines and tetramines useful as curing agents for epoxy resins are prepd. by cyanoethylating a cycloaliph. diamine and reducing the CN groups. Thus, 66 cm³ acrylonitrile [107-13-1] was added dropwise to 57 g 1,2-diaminocyclohexane [694-83-7] contg. 0.3 cm³ HOAc at .ltoreq.115.degree.. The mixt. was heated 1 h at 120.degree. to give N,N'-di(2-cyanoethyl)-1,2-diaminocyclohexane (I) [70476-20-9]. I was hydrogenated in the presence of Raney Ni to give N,N'-di(3-aminopropyl)-1,2-diaminocyclohexane (II) [72063-04-8]. A compn. contg. 100 parts bisphenol A diglycidyl ether polymer [25085-99-8] and 25 parts II was cured in a mold 2 h at 80.degree. and 2 h at 150.degree.. The cured resin had heat deflection temp. 121.5.degree. under 264 psi stress at heating rate 5.degree./min.

IT 72063-04-8

RL: MOA (Modifier or additive use); USES (Uses)
 (crosslinking agents, for epoxy resins)

RN 72063-04-8 CAPLUS

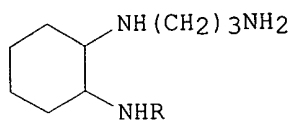
CN 1,2-Cyclohexanediamine, N,N'-bis(3-aminopropyl)- (9CI) (CA INDEX NAME)



L23 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 7
 ACCESSION NUMBER: 1980:8747 CAPLUS
 DOCUMENT NUMBER: 92:8747
 TITLE: Additives for lubricants and fuels
 INVENTOR(S): Kluger, Edward W.; Miley, John W.; Su, Tien K.
 PATENT ASSIGNEE(S): Milliken Research Corp., USA
 SOURCE: U.S., 6 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4153567	A	19790508	US 1977-850457	19771110

GI



I

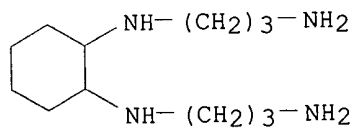
AB Dispersant additives for fuels and lubricating oils are manufd. by reacting I [$\text{R} = \text{H}, \text{H}_2\text{N}(\text{CH}_2)_3$] with a C.g.toreq.12 aliph. group-substituted polycarboxylic acid anhydride acylating agent (e.g., an olefin polymer-substituted succinic anhydride). Thus, 19.9 N,N'-bis(3-aminopropyl)-1,2-diaminocyclohexane [I; $\text{R} = \text{H}_2\text{N}(\text{CH}_2)_3$] [72063-04-8] and 31 g alkenylsuccinic anhydride (356 av. mol. wt.) were heated in PhMe at reflux for 14 h, and the H_2O produced was removed by a Dean Stark trap. Removal of the PhMe gave a viscous dispersant (97% yield). A mixt. (80 g) contg. mineral oil (7.7 cSt kinematic viscosity at 100.degree. F), 1 carbon black (24 mm particle size), and 15 g glass beads was centrifuged for 30 s at 3000 rpm and substantially complete pptn. of the carbon black occurred. The carbon black remained substantially uniformly dispersed under the same conditions when the mixt. contained 1.00% of the dispersant additive.

IT 72063-04-8D, reaction products with alkylsuccinic anhydrides
 RL: USES (Uses)

(dispersants, for fuels and lubricating oils)

RN 72063-04-8 CAPLUS

CN 1,2-Cyclohexanediamine, N,N'-bis(3-aminopropyl)- (9CI) (CA INDEX NAME)



L23 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:892726 CAPLUS
 DOCUMENT NUMBER: 134:172685

TITLE: Polyamine analogue antidiarrheals: A structure-activity study
 AUTHOR(S): Bergeron, Raymond J.; Wiegand, Jan; McManis, James S.; Weimar, William R.; Smith, Richard E.; Algee, Samuel E.; Fannin, Tammy L.; Slusher, Michael A.; Snyder, Patti S.
 CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida J. Hillis Miller Health Science Center, Gainesville, FL, 32610, USA
 SOURCE: Journal of Medicinal Chemistry (2001), 44(2), 232-244
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The syntheses of a group of spermine polyamine analogs and their evaluation as antidiarrheals are described. Each compd. was assessed in a rodent castor oil-induced diarrhea model for its ability to reduce stool output and wt. loss in a dose-dependent manner. The spermine pharmacophore is shown to be an excellent platform from which to construct antidiarrheals. The activity of the compds. is very dependent on both the nature of the terminal alkyl groups and the geometry of the methylene spacers sepg. the nitrogens. The toxicity profile is also quite dependent on these same structural features. On the basis of s.c. dose-response data and toxicity profiles, two compds., N1,N12-diisopropylspermine and N1,N12-diethylspermine, were taken forward into more complete evaluation. These measurements included formal acute and chronic toxicity trials, drug and metabolic tissue distribution studies, and assessment of the impact of these analogs on tissue polyamine pools. Finally, the remarkable activity of N,N'-bis[3-(ethylamino)propyl]-trans-1,4-cyclohexanediamine underscores the need to further explore this framework as a pharmacophore for the construction of other antidiarrheal agents.

IT 323582-94-1P

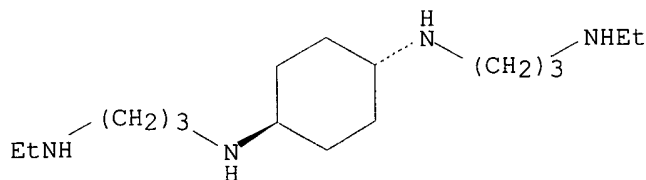
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(structure-activity relationship of antidiarrheal spermine polyamine analogs)

RN 323582-94-1 CAPLUS

CN 1,4-Cyclohexanediamine, N,N'-bis[3-(ethylamino)propyl]-, tetrahydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● 4 HCl

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:570940 CAPLUS

DOCUMENT NUMBER: 131:299436

TITLE: Optically active tetraazamacrocycles analogous to cyclam

AUTHOR(S): Alfonso, Ignacio; Astorga, Covadonga; Rebolledo, Francisca; Gotor, Vicente

CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Universidad de Oviedo, Oviedo, 33071, Spain

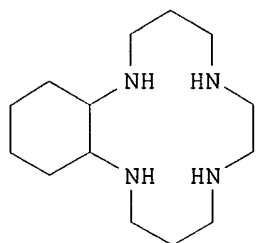
SOURCE: Tetrahedron: Asymmetry (1999), 10(13), 2515-2522
CODEN: TASYE3; ISSN: 0957-4166

PUBLISHER: Elsevier Science Ltd.

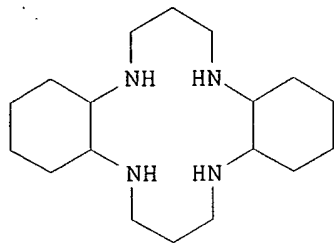
DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I



II

AB The syntheses of enantiopure tetraazamacrocycles analogous to cyclam, (S,S)-I, (R,R)-I, and (S,S,S,S)-II, have been carried out. NMR and semiempirical studies of I have revealed that this compd. presents a rigid conformation with C2 symmetry, which is stabilized by intramol. bifurcated hydrogen bonds. Structural studies for II have shown that the presence of two cyclohexane rings of (S,S) configuration leads to the loss of D2 symmetry in soln., which is in agreement with the AM1 calcd. structure.

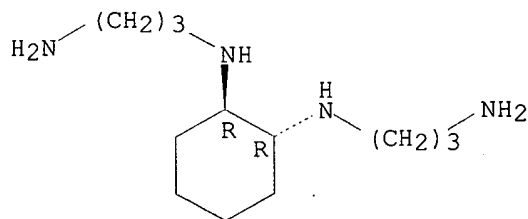
IT 186144-62-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(optically active tetraazamacrocycles analogous to cyclam)

RN 186144-62-7 CAPLUS

CN 1,2-Cyclohexanediamine, N,N'-bis(3-aminopropyl)-, tetrahydrochloride,
(1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



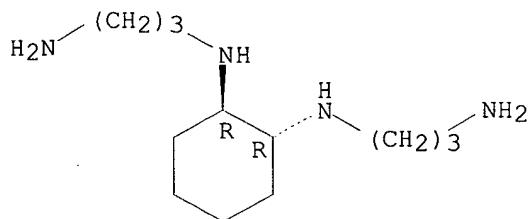
● 4 HCl

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:192748 CAPLUS
 DOCUMENT NUMBER: 130:325135
 TITLE: Chemoenzymatic syntheses of two optically active hexa-azamacrocycles
 AUTHOR(S): Alfonso, Ignacio; Rebolledo, Francisca; Gotor, Vicente
 CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Universidad de Oviedo, Oviedo, E-33071, Spain
 SOURCE: Tetrahedron: Asymmetry (1999), 10(2), 367-374
 CODEN: TASYE3; ISSN: 0957-4166
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Two optically active hexa-azamacrocycles with C2 and D2 symmetry, resp., were efficiently synthesized from an enzymically prepd. (R,R)-cyclohexane-1,2-diamine bis(amido ester) deriv.
 IT **186144-62-7P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (chemoenzymic prepn. of optically active hexaazamacrocycles)
 RN 186144-62-7 CAPLUS
 CN 1,2-Cyclohexanediamine, N,N'-bis(3-aminopropyl)-, tetrahydrochloride, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 4 HCl

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:268468 CAPLUS
 DOCUMENT NUMBER: 128:321505
 TITLE: synthesis and antineoplastic activity of conformationally restricted polyamines
 INVENTOR(S): Frydman, Benjamin J.; Marton, Laurence J.; Reddy, Vendohar K.; Valasinas, Aldonia L.; Witiak, Donald T.
 PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
 SOURCE: PCT Int. Appl., 92 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----

WO 9817624 A1 19980430 WO 1997-US18453 19971015
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
 AU 9749007 A1 19980515 AU 1997-49007 19971015
 EP 934249 A1 19990811 EP 1997-911695 19971015
 EP 934249 B1 20020327
 R: CH, DE, ES, FR, GB, IT, LI
 JP 2002508739 T2 20020319 JP 1998-519442 19971015
 PRIORITY APPLN. INFO.: US 1996-28680P P 19961018
 WO 1997-US18453 W 19971015

OTHER SOURCE(S): MARPAT 128:321505

AB Synthesis and antineoplastic activity of conformationally restricted polyamines (I) E-NH-D-NH-B-A-B-NH-D-NH-E (A = C2-C6 alkene, C3-C6 cycloalkyl, cycloalkenyl, or cycloaryl; B = independently a single bond, C1-C6 alkyl alkenyl; D = independently C1-C6 alkyl or alkenyl, or C3-C6 cycloalkyl, cycloalkenyl, or cycloaryl; E = independently H, C1-C6 alkyl or alkenyl) and pharmaceutically suitable salts thereof is reported. Thus, I [E = Et, D = (CH₂)₃, B = CH₂, A = cyclopropyl] .4HCl (II) is prepd. in five steps by LiAlH₄ redn. of di-Et 1,2-cyclopropyldicarboxylate, amination and HCl salt formation, mesitylsulfonylation, alkylation with BrCH₂CH₂CH₂N(SO₂Mes)Et and desulfonylation and HCl salt formation. II shows good cytotoxic activity against human tumor cell lines with an ID₅₀ of 0.12 .upsilon.g/mL against A549.

IT 206991-29-9P 206991-30-2P 206991-50-6P

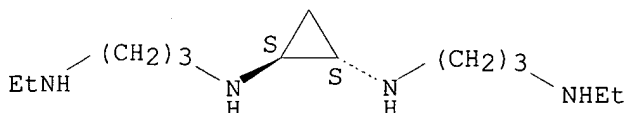
206991-51-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (synthesis and antineoplastic activity of conformationally restricted polyamines)

RN 206991-29-9 CAPLUS

CN 1,2-Cyclopropanediamine, N,N'-bis[3-(ethylamino)propyl]-, tetrahydrochloride, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

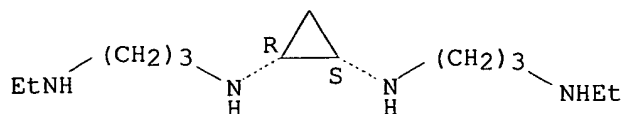


● 4 HCl

RN 206991-30-2 CAPLUS

CN 1,2-Cyclopropanediamine, N,N'-bis[3-(ethylamino)propyl]-, tetrahydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

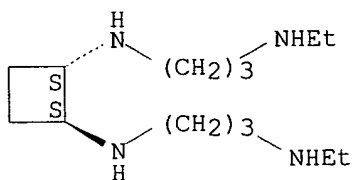
Relative stereochemistry.



●4 HCl

RN 206991-50-6 CAPLUS
 CN 1,2-Cyclobutanediimine, N,N'-bis[3-(ethylamino)propyl]-,
 tetrahydrochloride, (1R,2R)-rel- (9CI) (CA INDEX NAME)

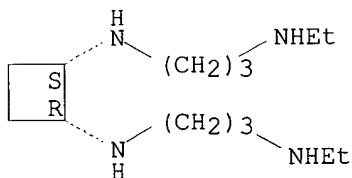
Relative stereochemistry.



●4 HCl

RN 206991-51-7 CAPLUS
 CN 1,2-Cyclobutanediimine, N,N'-bis[3-(ethylamino)propyl]-,
 tetrahydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



●4 HCl

L23 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:682957 CAPLUS
 DOCUMENT NUMBER: 130:52614
 TITLE: Conformationally Restricted Analogs of
 1N,12N-Bisethylspermine: Synthesis and Growth
 Inhibitory Effects on Human Tumor Cell Lines
 AUTHOR(S): Reddy, Venodhar K.; Valasinas, Aldonia; Sarkar,
 Aparajita; Basu, Hirak S.; Marton, Laurence J.;
 Frydman, Benjamin
 CORPORATE SOURCE: SLIL Biomedical Corp., Madison, WI, 53711, USA
 SOURCE: Journal of Medicinal Chemistry (1998), 41(24),

4723-4732

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Eight analogs of 1N,12N-bisethylspermine, (I), with restricted conformations were synthesized in the search for new spermine mimetics with cytotoxic activities. By replacing the central butane segment of I with a 1,2-disubstituted cyclopropane ring, a pair of cis/trans-isomers was obtained that introduced a spatial constraint in the otherwise freely mobile butane chain. An analogous pair of isomers was obtained when the butane segment was replaced with a 1,2-disubstituted cyclobutane ring or with a 2-butene residue. The six new analogs thus obtained (three pairs of cis/trans-isomers) were growth inhibitory at low-micromolar concns. against four human tumor cell lines (A549, HT-29, U251MG, and DU145) but were less growth inhibitory against two other human tumor cell lines (PC-3 and MCF7). 1N,12N-Bisethylspermyne, where the central butane segment of I was replaced by the rigid 2-butyne segment, was devoid of growth inhibitory activity against five of the six human cell lines studied (DU145 being the only exception), a clear indication of the importance of conformational mobility at the 4N,9N-butane segment of I for its biol. activity. When the butane segment was replaced by a benzene-1,2-dimethyl residue, the resulting analog was devoid of growth inhibitory activity despite its cisoid conformation. The cytotoxicity of the analogs does not seem to be directly related to their uptake by the cells or to their effects on cellular polyamine levels. Analogs of I with restricted conformations but which contained the equiv. of a two-carbon unit, rather than the natural four-carbon unit, at the central segment, such as 1,2-diaminocyclopropyl or 1,2-diaminocyclobutyl derivs., were devoid of growth inhibitory effects at the concns. studied. The development of conformationally restricted polyamine analogs appears to show promise in the further quest for polyamine-related therapeutic agents with specificity of action.

IT 206991-29-9P 206991-30-2P 206991-50-6P

206991-51-7P

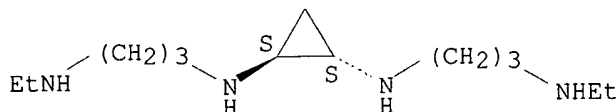
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and antitumor activity of bisethylspermine conformationally restricted analogs)

RN 206991-29-9 CAPLUS

CN 1,2-Cyclopropanediamine, N,N'-bis[3-(ethylamino)propyl]-, tetrahydrochloride, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

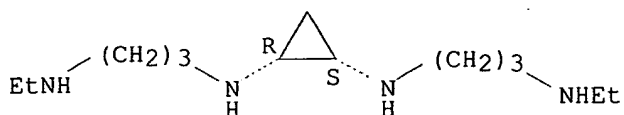


●4 HCl

RN 206991-30-2 CAPLUS

CN 1,2-Cyclopropanediamine, N,N'-bis[3-(ethylamino)propyl]-, tetrahydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

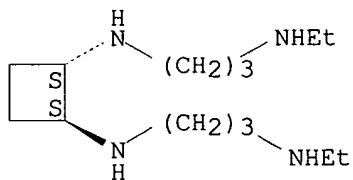
Relative stereochemistry.



● 4 HCl

RN 206991-50-6 CAPLUS
 CN 1,2-Cyclobutanediimine, N,N'-bis[3-(ethylamino)propyl]-,
 tetrahydrochloride, (1R,2R)-rel- (9CI) (CA INDEX NAME)

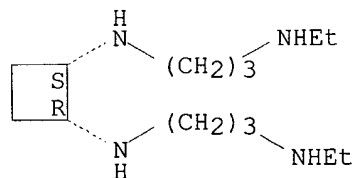
Relative stereochemistry.



● 4 HCl

RN 206991-51-7 CAPLUS
 CN 1,2-Cyclobutanediimine, N,N'-bis[3-(ethylamino)propyl]-,
 tetrahydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● 4 HCl

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:374955 CAPLUS

DOCUMENT NUMBER: 129:117029

TITLE: Preparation and spectral properties of nickel(II) and copper(II) complexes with two isomeric cyclohexylcyclams

AUTHOR(S): Sakata, Kazunori; Odamura, Takeharu; Kanbara, Yumie; Nibu, Tamami; Hashimoto, Mamoru; Tsuge, Akihiko; Moriguchi, Yoshiaki

CORPORATE SOURCE: Department of Chemistry, Faculty of Engineering,
Kyushu Institute of Technology, Kitakyushu, 804, Japan
SOURCE: Polyhedron (1998), 17(9), 1463-1470
CODEN: PLYHDE; ISSN: 0277-5387
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Ni(II) complexes of two isomeric cyclohexylcyclams were prep'd. by employing a Ni template reaction. The cyclohexylcyclams were synthesized from the Ni(II) complexes and then the Cu(II) complexes were prep'd. from the free ligands and Cu(II) perchlorate. The Ni(II) and Cu(II) complexes exhibit clusters of ions corresponding to $[M-ClO_4]^+$ and $[M-2ClO_4+2H]^+$ which is the base peak in FAB mass spectra. A strong band obs'd. at .apprx.3200 cm^{-1} is assigned to the N-H stretching mode and the band is slightly shifted to lower frequency on metal coordination, indicating freshly strong bands due to ClO_4^- stretching mode at .apprx.1090 and .apprx.620 cm^{-1} . The molar conductances for the complexes are 1:2 electrolytes in DMF and the perchlorate anions are ionized on dissoln. in the solvent. The Ni(II) and Cu(II) complexes of the two isomers are subjected to the square-planar ligand-field, but the ligand-field band for the Ni(II) complex of isomer Lt3, trans-cyclohexylcyclam, shows the distorted octahedral form in coordinating solvent. ESR spectra for the Cu(II) complexes of the two isomers also give the spin Hamiltonian parameters of the square-planar coordination. ^{13}C -NMR spectral results are comparable with those of another spectra.

IT 139559-15-2P 139559-16-3P

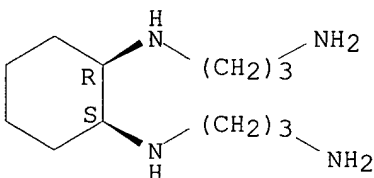
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(for prepn. of cyclohexylcyclam and its copper and nickel complexes)

RN 139559-15-2 CAPLUS

CN 1,2-Cyclohexanediamine, N,N'-bis(3-aminopropyl)-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

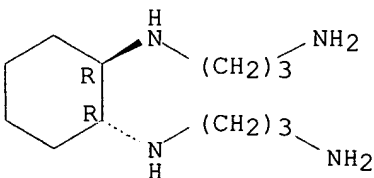
Relative stereochemistry.



RN 139559-16-3 CAPLUS

CN 1,2-Cyclohexanediamine, N,N'-bis(3-aminopropyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L23 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:668497 CAPLUS
 DOCUMENT NUMBER: 130:32686
 TITLE: QSAR analysis of polyamine transport inhibitors in L1210 cells
 AUTHOR(S): Xia, Cindy Q.; Yang, Johnny J.; Ren, Shijun; Lien, Eric J.
 CORPORATE SOURCE: Department Pharmaceutical Sciences, School Pharmacy, University Southern California, Los Angeles, CA, 90033, USA
 SOURCE: Journal of Drug Targeting (1998), 6(1), 65-77
 CODEN: JDTAEH; ISSN: 1061-186X
 PUBLISHER: Harwood Academic Publishers
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB In this paper, the authors attempt to construct a math. model to correlate the biol. activities of 63 polyamine transport inhibitors in L1210 cells with their physicochem. parameters. The inhibitory consts. (Ki) were obtained from the published work of Bergeron et al. Non-weighted least square method was used in deriving the regression equations with a BMDP program. An AM1 subroutine of the HyperChem program was used to optimize the geometry and calc. the mol. dipole moments and the distance between 2 terminal amino groups. A CQSAR program was used to calc. Clog P (oct./w.). A good correlation was obtained by a 5-parameter equation including the distance between 2 terminal amino groups (d), the no. of cationic charge (Charge), mol. wt. (MW), dipole moment (.mu.), and hydrogen bond forming ability (Hb). This model accounts for 81% of the variance in the data and can be used to est. transport-inhibitory activity of many other polyamine analogs. It gives some quant. information about the relationship between the polyamine analogs function as transport inhibitors and their mol. structures.

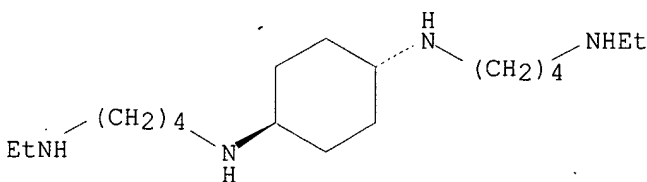
IT 177798-15-1 216577-73-0

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (QSAR anal. of polyamine transport inhibitors in L1210 cells)

RN 177798-15-1 CAPLUS

CN 1,4-Cyclohexanediamine, N,N'-bis[4-(ethylamino)butyl]-, trans- (9CI) (CA INDEX NAME)

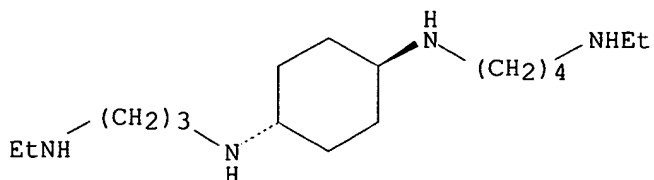
Relative stereochemistry.



RN 216577-73-0 CAPLUS

CN 1,4-Cyclohexanediamine, N-[4-(ethylamino)butyl]-N'-[3-(ethylamino)propyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:688058 CAPLUS

DOCUMENT NUMBER: 126:117748

TITLE: Sequential biocatalytic resolution of (+-)-trans-cyclohexane-1,2-diamine. Chemoenzymic synthesis of an optically active polyamine

AUTHOR(S): Alfonso, Ignacio; Astorga, Covadonga; Rebolledo, Francisca; Gotor, Vicente

CORPORATE SOURCE: Dep. Quim. Org. Inorg., Univ. Oviedo, Oviedo, 33071, Spain

SOURCE: Chemical Communications (Cambridge) (1996), (21), 2471-2472

CODEN: CHCOFS; ISSN: 1359-7345

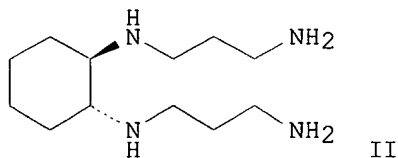
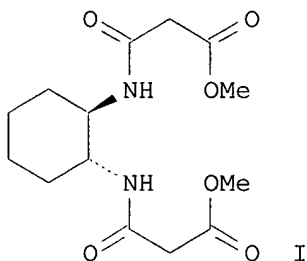
PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 126:117748

GI



AB *Candida antarctica* lipase-catalyzed double monoaminolysis of di-Me malonate by (+-)-trans-cyclohexane-1,2-diamine allows the sequential resolu. of the latter compd., affording enantiopure bis(amidoester) (R,R)-I, which is subsequently transformed into optically active polyamine (R,R)-II.

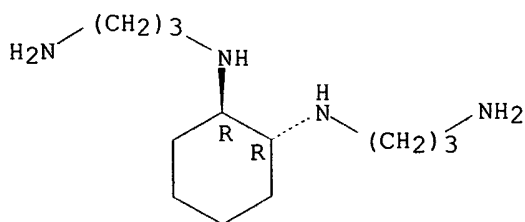
IT **186144-62-7P**

RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(sequential biocatalytic resolu. of trans-cyclohexanediamine in prepn. of optically active polyamine)

RN 186144-62-7 CAPLUS

CN 1,2-Cyclohexanediamine, N,N'-bis(3-aminopropyl)-, tetrahydrochloride, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 4 HCl

L23 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:328281 CAPLUS

DOCUMENT NUMBER: 125:25633

TITLE: Metabolically Programmed Polyamine Analog
Antidiarrheals

AUTHOR(S): Bergeron, Raymond J.; Yao, Guo Wei; Yao, Hua; Weimar, William R.; Sninsky, Charles A.; Raisler, Brian; Feng, Yang; Wu, Qianhong; Gao, Fenglan

CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida, Gainesville, FL, 32610, USA

SOURCE: Journal of Medicinal Chemistry (1996), 39(13), 2461-2471

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The design, synthesis, and testing of a novel class of antidiarrheal drugs based on a tetraamine pharmacophore are reported. While N1,N14-diethylhomospermine (DEHSPM) (5 mg/kg) completely prevents diarrhea in rodents, tissue distribution studies demonstrated that the principal metabolite of DEHSPM, homospermine (HSPM), accumulates and persists in tissues for a protracted period of time. This accumulation accounts for a large part of the chronic toxicity of DEHSPM. Thus a major objective was to develop a metabolically labile analog of DEHSPM which retained the desirable biol. properties of the parent drug. Hydroxyl groups, sites vulnerable to further metabolic transformation, were introduced into the external aminobutyl segments providing N1,N14-diethyl-(3R), (12R)-dihydroxyhomospermine [(HO)2DEHSPM]. The design concept was assisted by mol. modeling, which predicted that (HO)2DEHSPM would have a Ki for polyamine transport essentially identical with that of DEHSPM. The exptl. measured Ki and also the obsd. values of other biol. properties of (HO)2DEHSPM were in fact identical with those of DEHSPM, including IC50 against L1210 cells, impact on the NMDA receptor, and impact on L1210 native polyamine pools. Most significantly, however, there was no accumulation of the dideethylated metabolite in tissues from mice treated chronically with (HO)2DEHSPM, and (HO)2DEHSPM was 3-fold less toxic than DEHSPM. Finally, (HO)2DEHSPM completely prevented diarrhea in the castor oil-treated rat model at a dose of 5 mg/kg, just as did DEHSPM.

IT 177798-15-1 177798-16-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

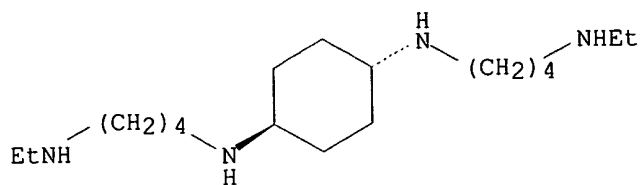
(synthesis and structure-activity relations for antidiarrheal polyamine analogs)

RN 177798-15-1 CAPLUS

CN 1,4-Cyclohexanediamine, N,N'-bis[4-(ethylamino)butyl]-, trans- (9CI) (CA

INDEX NAME)

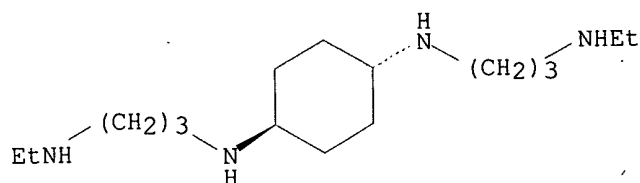
Relative stereochemistry.



RN 177798-16-2 CAPLUS

CN 1,4-Cyclohexanediamine, N,N'-bis[3-(ethylamino)propyl]-, trans- (9CI) (CA
INDEX NAME)

Relative stereochemistry.



L23 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:419120 CAPLUS

DOCUMENT NUMBER: 117:19120

TITLE: Synthesis and molecular structures of nickel(II)

alkyl-substituted cyclam complexes

AUTHOR(S): Kobiro, Kazuya; Nakayama, Atsuyoshi; Hiro, Toshitaka;
Suwa, Mitsuhiro; Tobe, Yoshito

CORPORATE SOURCE: Fac. Eng., Osaka Univ., Suita, 565, Japan

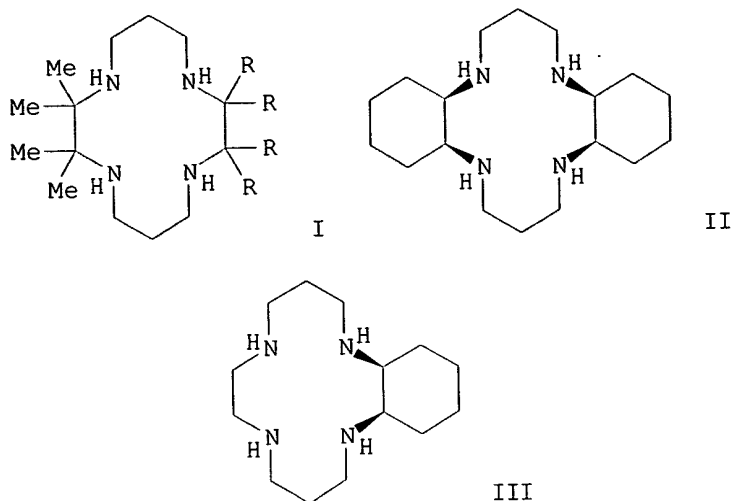
SOURCE: Inorg. Chem. (1992), 31(4), 676-85

CODEN: INOCAJ; ISSN: 0020-1669

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB Sterically congested cyclam derivs. II (R = Me, H) II, 3a (asym. cis isomer of II), III, and 5t (trans isomer of III) and their Ni(II) complexes have been synthesized. Magnetic susceptibility measurements of the complexes in the solid state and in water soln. indicate that the less congested complexes Ni(cyclam) $^{2+}$ and Ni(5t) $^{2+}$ are high-spin species in the solid state and Ni(cyclam) $^{2+}$, Ni(III) $^{2+}$, and Ni(5t) $^{2+}$ are mixts. of high-spin species and low-spin species in soln. On the other hand, highly congested complexes Ni(I) $^{2+}$ (R = Me, H) and Ni(II) $^{2+}$ are low-spin species in both the solid state and in soln. Ni(3a) $^{2+}$ is a high-spin species in the solid state, while it is a low-spin species in soln. Electronic spectra of Ni(cyclam) $^{2+}$, Ni(I) $^{2+}$ (R = Me, H), Ni(II) $^{2+}$, Ni(3a) $^{2+}$, Ni(III) $^{2+}$, and Ni(5t) $^{2+}$ measured in H₂O and in 5M NaClO₄ soln. supported the above observations. Half-wave potentials for the NiII/NiIII redox change (E_{1/2}(NiII,III)) were detd. for NiLX₂ (L = cyclam, I, II, 3a, III, 5t; X = NO₃, ClO₄, Cl). Ni(II) complexes with sterically congested ligands (Ni(I) $^{2+}$, Ni(II) $^{2+}$, Ni(3a) $^{2+}$ show higher half-wave potentials than those of the complexes with less congested ligands (Ni(cyclam) $^{2+}$, Ni(5t) $^{2+}$, Ni(III) $^{2+}$). Mol. structures of Ni(I)(NO₃)₂ (R = Me), Ni(II)(NO₃)₂, Ni(3a)(NO₃)₂, Ni(I)(NO₃)₂.cnddot.H₂O (R = H), and Ni(5t)(NO₃)₂ were detd. by x-ray crystal structure analyses, and the steric effects of the peripheral substituents on the coordination are discussed. In Ni(5t)(NO₃)₂, two axial nitrate anions coordinate to the central Ni atom to give six-coordinate octahedral geometry, while in Ni(I)(NO₃)₂.cnddot.H₂O (R = H) one axial nitrate anion semicoordinates to the central Ni atom to give five-coordinate square pyramidal geometry. Two types of unique structures exist in a unit cell of Ni(I)(NO₃)₂ (R = Me). One of the structures has four-coordinate square planar geometry, while in the other structure one axial nitrate anion semicoordinates to the central Ni atom to give a five-coordinate square pyramidal geometry around the Ni atom. Ni(3a)(NO₃)₂ possesses six-coordinate octahedral geometry, while Ni(II)(NO₃)₂ has four-coordinate square planar geometry with trans-I geometry of the cyclam ring.

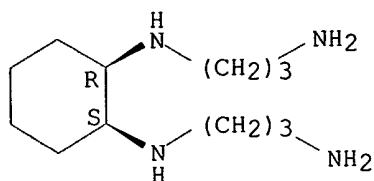
IT 139559-15-2P 139559-16-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and cyclocondensation reaction of, with glyoxal, in presence of nickel perchlorate with subsequent hydrogenation by borohydride)

RN 139559-15-2 CAPLUS

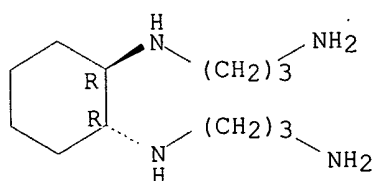
CN 1,2-Cyclohexanediamine, N,N'-bis(3-aminopropyl)-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 139559-16-3 CAPLUS
 CN 1,2-Cyclohexanediamine, N,N'-bis(3-aminopropyl)-, (1R,2R)-rel- (9CI) (CA
 INDEX NAME)

Relative stereochemistry.



L23 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1972:558116 CAPLUS

DOCUMENT NUMBER: 77:158116

TITLE: Stereochemical studies of metal chelates. VIII.

Absolute configuration and circular dichroism of cobalt(III) complexes with 4,7-diaza-1,10-diaminodecane (3,2,3-tet) derivatives

AUTHOR(S): Saburi, M.; Hattori, C.; Yoshikawa, S.

CORPORATE SOURCE: Fac. Eng., Univ. Tokyo, Tokyo, Japan

SOURCE: Inorg. Chim. Acta (1972), 6(3), 427-34

CODEN: ICHAA3

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Optically active tetradentate ligands, N,N'-bis-(.gamma.-aminopropyl)-R-1,2-diaminopropane (R-apbn), N,N'-bis(.gamma.-aminopropyl)-R-1,2-diaminocyclohexane (R-apchn), and N,N'-bis(.gamma.-aminopropyl)-(R)-2,3-diaminobutane ((R)-apbn; optical purity, 10%) were prepd. The trans-dichlorocobalt(III) complexes and oxalatocobalt(III) complexes with these ligands were prepd. and characterized. The (-)d-trans-Co(3,2,3-tet)Cl₂⁺ ion had the SS abs. configuration with respect to the coordinated secondary N centers, based on the similarity in the CD curves of this ion, and the R-apbn and R-apchn complexes. The SS abs. configuration of the latter complexes was estd. on the basis of the stereospecificity expected for the used asymmetric ligands. The topology of the oxalato (ox) complexes with 3,2,3-tet and its derivs. was detd. as the cis-.beta. structure from the PMR spectrum of Co((R)-apbn)ox⁺ ion.

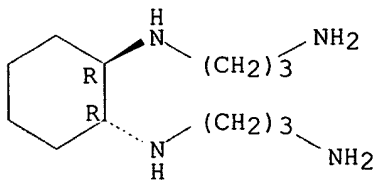
IT 38872-94-5P

RL: PREP (Preparation)
 (prepn. of)

RN 38872-94-5 CAPLUS

CN 1,2-Cyclohexanediamine, N,N'-bis(3-aminopropyl)-, (1R-trans)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 19 OF 19 USPATFULL

ACCESSION NUMBER: 2002:116446 USPATFULL
 TITLE: Conformationally restricted polyamines
 INVENTOR(S): Frydman, Benjamin J., Madison, WI, United States
 Marton, Laurence J., Fitchburg, WI, United States
 Reddy, Venodhar K., Madison, WI, United States
 Valasinas, Aldonia L., Madison, WI, United States
 Witiak, Donald T., Madison, WI, United States
 PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, Madison, WI,
 United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6392098	B1	20020521
APPLICATION INFO.:	US 1999-280278		19990329 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1997-951015, filed on 15 Oct 1997, now patented, Pat. No. US 5889061		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Barts, Samuel		
LEGAL REPRESENTATIVE:	Leone, Esq., Joseph T., DeWitt Ross & Stevens S.C.		
NUMBER OF CLAIMS:	22		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	32 Drawing Figure(s); 20 Drawing Page(s)		
LINE COUNT:	1578		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			
AB Compounds of Formula I:			

E--NH--D--NH--B--A--B--NH--D--NH--E (I)

wherein A is C.sub.2-C.sub.6 alkene, C.sub.3-C.sub.6 cycloalkyl, cycloalkenyl, or cycloaryl; B is independently a single bond, C.sub.1-C.sub.6 alkyl alkenyl; D is independently C.sub.1-C.sub.6 alkyl or alkenyl, or C.sub.3-C.sub.6 cycloalkyl, cycloalkenyl, or cycloaryl; and E is independently H, C.sub.3-C.sub.6 alkyl or alkenyl; and pharmaceutically-suitable salts thereof; a synthetic method therefor, pharmaceutical dosage forms containing one or more of these compounds, and use of these compounds in the treatment of neoplastic cell growth, are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

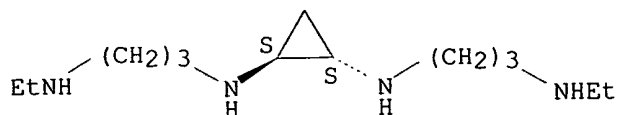
IT 206991-29-9P 206991-30-2P 206991-50-6P
 206991-51-7P

(prepn. of conformationally restricted spermine analogs as antineoplastic agents)

RN 206991-29-9 USPATFULL

CN 1,2-Cyclopropanediamine, N,N'-bis[3-(ethylamino)propyl]-, tetrahydrochloride, (1R,2R)-rel- (9CI) (CA INDEX NAME)

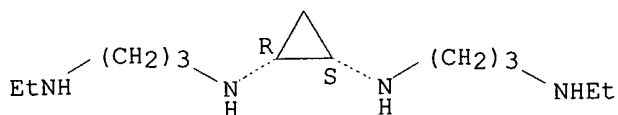
Relative stereochemistry.



● 4 HCl

RN 206991-30-2 USPATFULL
 CN 1,2-Cyclopropanediamine, N,N'-bis[3-(ethylamino)propyl]-,
 tetrahydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

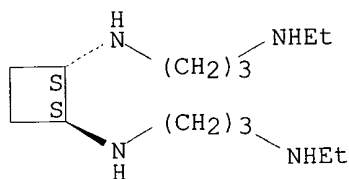
Relative stereochemistry.



● 4 HCl

RN 206991-50-6 USPATFULL
 CN 1,2-Cyclobutanediamine, N,N'-bis[3-(ethylamino)propyl]-,
 tetrahydrochloride, (1R,2R)-rel- (9CI) (CA INDEX NAME)

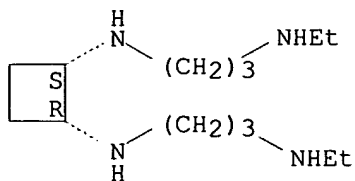
Relative stereochemistry.



● 4 HCl

RN 206991-51-7 USPATFULL
 CN 1,2-Cyclobutanediamine, N,N'-bis[3-(ethylamino)propyl]-,
 tetrahydrochloride, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



●4 HCl

=> file caold; d que nos 120

FILE 'CAOLD' ENTERED AT 16:04:31 ON 15 AUG 2002

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1907-1966

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L7	SCR 1007
L8	SCR 1236
L12	STR
L14	SCR 1839
L16	19 SEA FILE=REGISTRY SSS FUL L12 AND L7 AND L8 NOT L14
L20	0 SEA FILE=CAOLD ABB=ON PLU=ON L16

=> file home

FILE 'HOME' ENTERED AT 16:04:33 ON 15 AUG 2002